

**UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS**

FEDERAL TRADE COMMISSION,

Plaintiff,

v.

DIRECT MARKETING CONCEPTS, INC, et
al,

Defendants

CIVIL ACTION NO. 04-CV 11136GAO

**DECLARATION OF FRANK I. GREENWAY, M.D.,
IN RESPONSE TO THE DECLARATION OF MARY LEE VANCE, M.D.,
REGARDING HER REVIEW OF RENUVA™ AND ITS INGREDIENTS**

I, Frank L. Greenway, hereby declare as follows:

Introduction and Qualification

1. My education consists of a Bachelor's degree in Biology from Stanford University, Palo Alto, California, and a Doctor of Medicine degree from the University of California at Los Angeles, Los Angeles, California. I did a rotating internship with an emphasis in internal medicine, a residency in internal medicine, a chief residency and fellowship in endocrinology and metabolism all at Harbor-UCLA Medical Center in Torrance, California. I am board certified in both internal medicine and in endocrinology and metabolism.
2. I am presently the Medical Director and a Professor at Pennington Biomedical Research Center, a research campus of Louisiana State University in Baton Rouge, Louisiana. I direct the outpatient research clinic and the focus of research at the Pennington Biomedical Research Center in obesity and its associated medical problems. There are presently two grants funded by the National Institute of Aging that are being executed in our clinical area. One is on the effect of calorie restriction on measures of aging and the other seeks to learn the attributes that are characteristic of healthy people over 90 years of age.

3. I was in clinical practice of internal medicine and endocrinology in Marina del Rey, California for 20 years. During that time I also taught part-time at UCLA and did clinical research from the practice setting. During that time, I rose from instructor to Clinical Professor at the UCLA School of Medicine. In 1995, I assumed my present position at the Pennington Biomedical Research Center.
4. I have published over 60 peer-reviewed original research articles and over 20 chapters and reviews. I have grants from the food, nutraceutical and pharmaceutical industries in addition to funding from the National Institutes of Health. I have 4 issued patents and 4 other patent applications that are pending approval.
5. I belong to several scientific societies, am a Fellow and have held offices in the North American Association for the Study of Obesity, am a reviewer for several scientific journals and am a Fellow of the American College of Physicians. I received a reward for teaching from Harbor-UCLA Medical Center and have taught continuing medical education courses and advised graduate students, since coming to the Pennington Biomedical Research Center.
6. An accurate and current curriculum vitae is provided as an addendum to this Declaration.

Background and Discussion Regarding the Mechanism of Action of the Renuva™ System

1. Growth hormone levels decrease with aging and low growth hormone levels result in decreased energy and stamina, decreased lean body mass, compromised skin texture, an erosion of cognitive powers and memory, and other effects mentioned in the infomercial. People who are growth hormone deficient have an IGF-1 level of less than 350 U/L. Less than 5% of the population in the 20-40 year age group have growth hormone deficiency, but 30% of those over 60 years of age are growth hormone deficient. The implications of being partially deficient (>350 U/L but less than a normal for a younger age) are not definitely known, but since growth hormone decreases with age, it is reasonable to assume that partial deficiency is common and that those with partial deficiency would be likely to benefit from optimal levels of growth hormone.

2. Treating growth hormone deficiency has been demonstrated to reverse many of these undesirable physiological effects that are attributed to aging. The aging characteristics that have been shown to be reversed by the replacement of GH include those presented in the infomercial: increased energy, increased stamina, increased lean body mass, improved skin texture, improved memory and improved cognition.
3. Growth hormone releasing hormone (GHRH) is primarily responsible for the secretion of growth hormone. Other peptides, growth hormone releasing peptides (GHRP), are also capable of causing this secretion. The Infuser contains a dose of 1,500 nanograms of growth hormone releasing peptides 2 and 6 per daily dose (information from Anti-Aging Formulas) complexed in a proprietary delivery-system polymer (macro-molecular complex) that the University of Illinois has demonstrated to have the ability to transport large molecules across membranes. The macro-molecular complex delivers large proteins and polypeptides efficiently into the blood stream in a time-release manner to mimic intravenous infusion pharmacokinetics. The delivery of polypeptides across the mucosa when combined with the macro-molecular complex is 90% efficient (information from Anti-Aging Formulas). Thus, 1,350 nanograms of growth hormone releasing peptide should be released into the blood stream in a time-release manner from this 1,500 nanogram dose. Infusion of growth hormone releasing hormone at 2.5 ng/kg/min increases growth hormone significantly in man (Sassolas et al , 1986). This dose is equivalent to 175 ng/min in a 70 kg man. Acute doses of growth hormone releasing hormone and growth hormone releasing peptide 2 of 1 microgram/kg each increase growth hormone significantly in man (Pihoker C. et al., 1997). The acute doses of growth hormone releasing hormone and growth hormone releasing peptides required to increase growth hormone are, therefore, similar. Thus, one could reasonably presume that an infusion of growth hormone releasing peptide at 2.5 ng/kg/min would increase growth hormone, since this dose of growth hormone releasing hormone was sufficient to do so. The 1,350 nanograms of growth releasing peptide delivered by the Infuser would presumably be the equivalent of an 8-minute infusion of growth hormone releasing hormone or growth hormone releasing peptide at 175ng/min or 2.5 ng/kg/min in a 70 kg man

- 4 The proprietary delivery system developed by the University of Illinois is capable of not only transporting growth hormone releasing peptides into the blood in a manner mimicking intravenous infusion, but it is also capable of facilitating passage across the blood-brain barrier. Since the University of Illinois has documented passage of intact human growth hormone, the smaller growth hormone releasing peptides should easily reach central sites where growth hormone is released.
- 5 Anti-Aging Formulas' Renuva Generator includes the following amino acids: Arginine 100 mg, glutamine 100 mg, glycine 100 mg, lysine 100 mg, ornithine 50 mg and glutamic acid 30 mg. The scientific literature suggests that growth hormone can be stimulated by the oral intake of the following amino acids: lysine 1200 mg with arginine 1200 mg (Isadori A et al. 1981), 2 grams of glutamine (Welbourne TC, 1995) or 5.6 grams of glycine (Kasai K et al., 1978). Since arginine is converted to ornithine, the ornithine in the Generator can be considered like arginine. The mixture of amino acids in the Generator formula is 17% of the amino acids needed to stimulate growth hormone orally without considering the growth hormone releasing peptides in the Infuser.

Review of the Declaration of Dr. Mary Lee Vance

1. Dr. Vance does not believe that the Company's reliance on published data generated from studies in which GH was injected into subjects is valid. She seems to believe that the GHRP (not GH) are being introduced to the body by absorption through the intestinal tract, requiring the GHRP to pass through the stomach and be subject to gastric acidity hydrolysis. However, the growth hormone releasing peptides are absorbed through the mucosa in the mouth. This prevents their degradation by gastric acid or by peptidases in the gastrointestinal tract. In fact, the Infuser is designed to deliver the growth hormone releasing peptides to the blood stream in a fashion that mimics intravenous infusion, and the macromolecular complex also facilitates its entry across the blood brain barrier where it can act to release growth hormone.
2. Dr. Vance also states that "there is no evidence that sublingual or oral administration of arginine (a key ingredient in the Renuva Generator) significantly increases sustained serum GH or IGF-1 levels." Dr. Vance also states that she is not aware of any clinical trial evidence showing that the ingredients in the

Renuva powder increase GH..." There is a significant amount of clinical data that supports the position that the ingredients of the Renuva Generator does in fact increase ones own HGH. In fact, one study gave oral arginine 9 grams or a placebo daily to 10 post-menopausal women for 1 month with cross-over to the alternate treatment after a 1 month washout. L-arginine increased growth hormone (1.5 ± 1.8 mg/L vs. 0.6 ± 0.6 mg/L, $p<0.04$) demonstrating a sustained increase of growth hormone over 1 month with oral arginine (Blum A. et al., 2000).

3. Based on information that the acute administration of growth hormone releasing peptides and growth hormone releasing hormone release growth hormone at a similar doses to stimulate growth hormone secretion, it is reasonable to presume that growth hormone releasing peptide would stimulate growth hormone at 2.5ng/kg/min infusion, since such was found with that dose of a growth hormone releasing hormone infusion. Since the Infuser contains 1500 nanograms of growth hormone releasing peptides that are 90% absorbed, it is reasonable to assume this might cause the release of growth hormone since it is equivalent to an 8-minute infusion at 2.5ng/kg/min in a 70 kg man. Since the Generator contains 17% of the amino acids required to stimulate growth hormone orally, it is reasonable to assume that the Generator would give the Infuser a helping hand and aid in stimulating growth hormone.

In my opinion, after evaluating the ingredients in the Renuva System, I believe that it is reasonable to hypothesize that the Renuva system could be effective in stimulating endogenous growth hormone secretion with all the relevant advantages associated with such an increase. It is not unreasonable to assume that the use of the Renuva System would cause a measurable increase in growth hormone and/or IGF-1.

I hereby declare under penalty of perjury that the foregoing is true and correct to the best of my knowledge.

Signed: Frank Greenway

Date: 6/8/05